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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,874	12/11/2001	Edward B. Goldberg	NANF.P-007	4607

21121 7590 11/01/2005

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,874	GOLDBERG, EDWARD B.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46,49,50 and 66-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46,49,50 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 08/10/05 has been acknowledged.

Claims 1-45, 47-48 and 51-65 are canceled.
Claims 66-101 are newly filed.
Claims 46, 49-50 and 66-101 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 102

Claim 46 stand rejected under 35 U.S.C. 102(b) as being anticipated Cerritelli et al, J. Mol. Bio. 260:767-780,1996, for the same reasons of record as set forth in the office action mailed on 05/25/05.

The instant claim is drawn to a protein produced by growing cell containing a purified nucleic acid, comprising a nucleotide sequence encoding a gp35 protein. Given the broadest reasonable interpretation the scope of instant claim encompasses any protein produced by a host cell infected with T4 bacteriophage.

Cerritelli et al teaches stoichiometry and domaninal organization of long tail-fiber (LTF) of T4 bacteriophage. Using electron microscopy, PAGE and computational sequence analysis the cited art establishes that the LTF comprises three copies each of gp34, gp37 and gp36 and one copy of gp35 (abstract, page 771, table-1). The cited art further teaches culture of *E. coli* host cells infected with T4 bacteriophage (page 778, col.1 para. 3). The cited art

further teaches purification of long tail-fibers, proximal half-fibers and distal half fibers from the cell lysate using DEAE-sepharose CL-6B column chromatography procedure (page 778, col.1 para.4). The cited art further teaches isolation of various LTF components (i.e. gp34, gp337, gp35 and gp36) by gel electrophoresis (page 771, fig-3). Besides other tail-fiber components the cited art teaches an isolated gp35 protein (fig-3, lane 2, band 3) which is identical to the product as claimed. Furthermore where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Response to arguments (35 USC 102)

The applicant arguments regarding prior art issue on page 7 of response filed on 08/10/05 has been fully considered. Regarding applicant's argument that claim 46 has been amended to specify that "hetrologous promoter is not a bacteriophage promoter", the argument has been found unpersuasive because claim 46 has not been amended as asserted by the applicant (see list of claims submitted on 08/10/05). The applicant further argues that combined with the requirement that the nucleic acid is "purified" prior to introduction to the host cell, this clearly excludes a protein that is mealy produced by a cell infected with T4. However, this is found not persuasive because if the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Thus the cited art clearly anticipate the invention as claimed.

Claims 66 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldberg (WO 96/11947, 1996).

Claims 66 and 67 are drawn to a purified composition comprising a gp35 or bacteriopahge T4 gp35 protein not contained in a gel. Goldberg teaches isolated polypeptide consisting essentially of bacteriphage T4 p35 protein (see page 48, page 55, line 15-36; page 60 lines 1-4). The cited art teaches the isolation of recombinant gp35 protein using standard chromatography techniques including gel filtration and affinity chromatography (page 20). Thus given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed, since the gp35 as claimed is not limited to a particular amino acid sequence.

Claim Rejections - 35 USC § 103

Claims 49-50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cerritelli et al, J. Mol. Bio. 260:767-780,1996 as applied to claim 46 above, and further in view of Huynh (US 5,151,165, 1992) for the same reasons of record as set forth in the office action mailed on 05/25/05.

> Even though Cerritelli et al teaches the isolation of a gp35 protein from T4 bacteriophage infected host cells, the cited art does not teach the isolation of the gp35 protein, wherein the protein is not contained in a gel.
>
> Huynh teaches a method and apparatus for preparative electrophoresis for the purification of proteins (col. 6 lines 9-54, Fig-1). The cited art teaches a method that involves continuous electrophoresis until the products emerge from the bottom of the gel. The cited art teaches that the lower surface of the gel, which marks the end of electrophoretic migration, comprises a membrane or porous body form the boundaries of an elution chamber through which a current of buffer flows and carries the products which have emerged from the gel to a fraction collector (col.1, lines 47-54).
>
> Thus it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify the teaching of Cerritelli who teaches isolation of gp35 protein by gel electrophoresis with Huynh who teaches purification and elution of protein by preparative electrophoresis. One would have been motivated to do so to obtain a highly purified protein preparation. One would have a reasonable expectation of success, since purification of protein via

preparative electrophoresis and in a desired quantity has been well within the reach of one ordinary skilled in the art at the time the instant invention was made. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Response to arguments (35 USC 103)

The applicant arguments regarding prior art issue on page 7 of response filed on 08/10/05 has been fully considered. Regarding applicant's argument that claims are not directed to a method for obtaining highly purified protein but to a protein as obtained, the argument has been found unpersuasive because instant claims encompasses a product as a result of purification which is indistinguishable from the cited prior art of record because if the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). Regarding applicant's argument that office has not shown anything about the properties of the protein out side a gel, the argument has been found unpersuasive because if the composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02.

In addition, it is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955): However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32

C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added).

Claim Rejections - 35 USC § 112

Claims 66-101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses a composition comprising any gp35 protein, bacteriophage T4 gp35 protein and any variant thereof. The scope of invention as claimed encompasses any variant of amino acid sequences encoding SEQ ID NO:2 with one or more conservative substitution relative to the amino acid sequences found in SEQ ID NO:2. The scope of invention as claimed further encompasses variants of SEQ ID NO:2 from amino acid numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 and 81-93 with one or more conservative substitutions relative to the amino acid sequence of SEQ ID NO:2 and having any functional activity. The scope of invention as claimed further encompasses variants of a protein encoded by SEQ ID NO: 2 that binds to the p34 protein of bacteriophage T4 or to an antibody directed against any gp35 protein (*not limited to gp35 of bacteriophage T4)* or a ligand. The variants as claimed further encompasses a molecule comprising amino acid sequences having at least 30% or 60% identity to amino acid numbers 57-93 in SEQ ID

NO:2 over 36 amino acid sequences. In addition the variants as claimed further encompasses a molecule comprising amino acid sequences having at least 60% identity to amino acid numbers 1-100 in SEQ ID NO:2 over 100 amino acid sequences.

At best the specification only disclose that the amino acid sequence of SEQ ID NO:2 which encodes the bacteriphage T4 gp35 protein. The specification disclosed that the phage T4 gp35 is located between genes gp34 and gp36. The specification further disclosed that two open reading frames ORF34.1 and ORF35 actually connect to form a single ORF35, which encodes a protein of about 40,000 Daltons. The specification further disclosed cloning of ORF35 by PCR of phage DNA between 5'-ATG start codon of ORF34.1 and 3'TAA stop codon of ORF35, which yield a sequence of approximately 1,120 nucleotides in length. However the specification as filed fails to disclose any variant of gp35 (other than SEQ ID NO:2) which has gp35 like activity explicitly or implicitly as putatively claimed herein. For example, the specification fails to disclose any other molecule (besides SEQ ID NO:2) comprising a T4 gp35 fragment consisting of amino acid sequences of 1-7, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93 obtained from SEQ ID NO:2 and attach to the C-terminus of bacteriophage T4 p34 (all organisms). Similarly the specification fails to disclose that isolated fragments consisting of amino acid sequences of 1-7, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93 obtained from SEQ ID NO:2 comprises a C-terminal gp36 binding domain (all organisms).

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only disclose that the amino acid sequence of SEQ ID NO:2 which encodes the bacteriphage T4 gp35 protein. The specification fails to disclose any other variant of SEQ ID NO:2 as putatively claimed herein. The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the

invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the gp35 or SEQ ID NO:2 variants (as claimed) has been defined only by a statement of function that broadly encompasses a bacteriphage T4 gp35 protein-like activity, an affinity for any gp35 antibody or an affinity for bacteriophage T4 gp34 protein, which conveyed no distinguishing information about the identity of the claimed gp35 protein or any variants thereof, such as its relevant structural or physical characteristics. The variation as claimed also encompasses variation in unknown number of conserved motifs. The specification fails to define what are the conserved amino acid sequences in SEQ ID NO:2, which one skill in the art would considered germane for any bacteriphage T4 gp35 protein activity.

Furthermore 40-70% variation (30-60% identity) as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. The specification fails to disclose that isolated fragments consisting of amino

acid sequences of 1-7, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93 obtained from SEQ ID NO:2 or any variant thereof (as claimed) attach to the C-terminus of bacteriophage T4 p34 and would have a bacteriophage T4 gp35 like activity. Similarly the specification fails to disclose that isolated fragments consisting of amino acid sequences of 1-7, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93 obtained from SEQ ID NO:2 or any variant thereof (as claimed) comprises a C-terminal gp36 binding domain (all organisms) would have a bacteriophage T4 gp35 like activity. Regarding claims 66-67 and 76-79 specifically the scope of invention as claimed encompasses a composition comprising any gp35 protein or bacteriophage T4 gp35 protein, since the polypeptides as claimed has not been identified by a structure (i.e. SEQ ID NO), therefore it is unclear what encompasses the claimed variant in this context. Even though the variants as claimed are limited to the amino acid sequence of SEQ ID NO:2, the variant as claimed encompasses a gp35-like protein with one or more [emphasis added] conservative substitutions, or 60% identity to SEQ D NO:2, or comprises at least 8 contiguous amino acids of SEQ ID NO:2, or bound to an antibody directed against gp35 and binds to p36 or p34, or comprises a fragment of SEQ ID NO:2 (see claim 18 and 19) with one or more conservative substitutions, or 30% or 60% identity to amino acid numbers 57-93 of SEQ ID NO:2, wherein the protein has a amino acid terminus that attaches to the C-terminus of bacteriophage T4 p34 protein. The specification as filed fails to disclose any variant of SEQ ID NO:2 having a functional activity of gp35 of bacteriophage T4. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 66-101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for bacteriphage T4 gp35 protein encoded by the amino acid sequences of SEQ ID NO:2, does not reasonably provide enablement for any gp35 protein any bactriophage T4 gp35 protein or any variants of SEQ ID NO:2 (as

claimed). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of Invention:

The instant invention relates to isolated bacteriphage T4 gp35 protein.

Breadth of Claims and Guidance Provided in the Specification:

The scope of invention as claimed encompasses a composition comprising any gp35 protein, bacteriophage T4 gp35 protein and any variant thereof. The scope of invention as claimed encompasses any variant of amino acid sequences encoding SEQ ID NO:2 with one or more conservative substitution relative to the amino acid sequences found in SEQ ID NO:2. The scope of invention as claimed further encompasses variants of SEQ ID NO:2 from amino acid numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 and 81-93 with one or more conservative substitutions relative to the amino acid sequence of SEQ ID NO:2 and having any functional activity. The scope of invention as claimed further encompasses variants of a protein encoded by SEQ ID NO: 2 that binds to the p34 protein of bacteriophage T4 or to an antibody directed against any gp35 protein *(not limited to gp35 of bacteriophage T4)* or a ligand. The variants as claimed further encompasses a molecule comprising amino acid sequences having at least 30% or 60% identity to amino acid numbers 57-93 in SEQ ID NO:2 over 36 amino acid sequences. In addition the variants as claimed further encompasses a molecule comprising amino acid sequences having at least 60% identity to amino acid numbers 1-100 in SEQ ID NO:2 over 100 amino acid sequences.

At best the specification only disclose that the amino acid sequence of SEQ ID NO:2 which encodes the bacteriphage T4 gp35 protein. The specification disclosed that the phage T4 gp35 is located between genes gp34 and gp36. The specification further disclosed that two open reading frames ORF34.1 and ORF35 actually connect to form a single ORF35, which encodes a protein of about 40,000 Daltons. The specification further disclosed cloning of ORF35 by PCR of phage DNA between 5'-ATG start codon of ORF34.1 and 3'TAA stop codon of ORF35, which yield a sequence of approximately 1,120 nucleotides in length. However the specification as filed fails to disclose any

variant of gp35 (other than SEQ ID NO:2) which has gp35 like activity explicitly or implicitly as putatively claimed herein. For example, the specification fails to disclose any other molecule (besides SEQ ID NO:2) comprising a T4 gp35 fragment consisting of amino acid sequences of 1-7, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93 obtained from SEQ ID NO:2 and attach to the C-terminus of bacteriophage T4 p34 (all organisms). Similarly the specification fails to disclose that isolated fragments consisting of amino acid sequences of 1-7, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93 obtained from SEQ ID NO:2 comprises a C-terminal gp36 binding domain (all organisms).

State of Art and Predictability

The bacteriophage T4 is one of the archetypical members of the family Myoviridae or T-even phage. These viruses are characterized by a large elongated icosohedral head, a contractile tail and tail fibers. The tail fiber proteins have an unusual quaternary structure of long, thin and rigid rods. Their function is to transduce chemical recognition of the E. coli host into a mechanical force on the phage base plate, essentially acting as a set of cooperative levers. This mechanical stress triggers a series of protein conformational changes that lead to entry of the phage DNA into the cell. The three main tail fiber proteins, P34, P36 and P37, are thought to be principally composed of dimeric anti parallel-sheets. *Gp35, which forms the angle in the tail fiber, probably has a more complex structure. The joints between the homodimeric segments are also likely to have a more complex structure but there is no evidence that the central rod regions have any tertiary structure at all.* The extended anti parallel-sheet secondary structure supports the rigid rod quaternary structure. (Hyman et al, PNAS 99(13): 8488-8493, 2002).

The instant application claims numerous variants of the bacteriophage T4 gp35 protein, but provides no distinguishing information about the identity of the claimed variants, such as its relevant structural or physical characteristics. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide

and its tertiary structure is neither well understood nor predictable. The variants as claimed herein are mere hypothetical possibilities because no biological functions have been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. For example the specification fails to provide any evidence that establishes that fragments of SEQ ID NO:2 or any variants of these fragments are capable of binding to C-terminal of T4 gp34 and N-terminal of gp36 (wherein gp36 is obtained from any organism) or to an antibody that recognizes the gp35 protein. Therefore, applicant has not presented enablement commensurate in scope with the claims. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Furthermore screening of any and all natural and non-natural variants, wherein any number of amino acid are added substituted and/or deleted at random in an amino acid sequence is not considered routine. Making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein at least 30-60% or more amino acids are added, deleted and/or substituted at random. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make and test the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed *bacteriophage T4 gp35-like activity*. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). The bacteriphage T4 gp35 protein which forms the angle in the tail fiber is known to have a

complex structure and without sufficient guidance to make a specific mutation in the disclosed amino acid sequences the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to practice the invention as claimed, since the applicant has not presented enablement commensurate in scope with the claims.

Claim 46 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the same reasons of record as set forth in the office action mailed on 05/25/05.

Claim 46 recites the limitation "The protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Response to arguments (35 USC 112(2))

Even though the applicant asserts that instant claim has been amended the applicant fails to amend claim 46 to over come this rejection (*see claims submitted on 08/10/05*).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

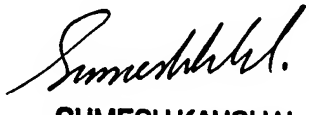
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

-sk



SUMESH KAUSHAL
PATENT EXAMINER